IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

Attorney Docket No.	KINE-001CIP5
Confirmation No.	5685
First Named Inventor	DEDHAR, SHOUKAT
Application Number	09/998,250
Filing Date	November 30, 2001
Group Art Unit	1617
Examiner Name	WILLIAMS, LEONARD M.
Title: *"TREATMENT OF INFLAMMATORY DISEASES INCLUDING PSORIASIS"*	

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

Sir:

This Brief is filed in support of Applicant's appeal from the Examiner's Rejection dated February 6, 2006. No claims have been allowed. Claim 1 is pending. Claims 2-14 have been cancelled. Claims 15-22 have been withdrawn from consideration. A Notice of Appeal was filed on August 1, 2006.

Appellants refer the attention of the Board to Appellants petition for review of the restriction requirement under 37 C.F.R. § 1.144, filed concurrently herewith. Appellants have petitioned for rejoinder of withdrawn Claims 15-20. To the extent that the Director responds favorably to the Appellants' petition, Claims 1 and 15-20 are appealed. Should the Director respond negatively to the Appellants' petition, then Claim 1 is appealed. Appellants note that the rejoinder of Claims 15-20 does not change the issues on appeal or the remarks presented herein below.

The Commissioner is hereby authorized to charge deposit account number 50-0815, reference no. KINE-001 CIP5 to cover any fee required under 37 C.F.R. §1.17(c) for filing Applicant's brief. Additionally, in the event that the fee transmittal or other papers are separated from this document and/or other fees or relief are required, the Appellant petitions for such relief, including extensions of time, and authorize the Commissioner to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to the above disclosed deposit account.

REAL PARTY IN INTEREST

The real party in interest is QLT Pharmaceuticals, Inc., which is an assignee and licensee of the invention, as evidenced by the assignment recorded on December 20, 2005, reel/frame 016923/0152, and Sunnybrook and Women's College and Health Sciences Centre, which is an assignee of the invention as evidenced by the assignment recorded March 28. 2002, reel and frame 012760/0837.

RELATED APPEALS AND INTERFERENCES

There are currently no other appeals or interferences known to Appellants, the undersigned Appellant's representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.

STATUS OF CLAIMS

The present application was filed on November 30, 2001 with 14 claims. In response to a Restriction Requirement was mailed on February 24, 2003, Appellants canceled Claims 11-12. A first Office Action was mailed on June 4, 2003. On August 28, 2003 in response to the Office Action, Appellants canceled Claim 3. A Final Rejection was mailed on March 8, 2004. On September 8, 2004, in response to the Final Rejection, the Appellants canceled Claims 2, 4-10 and 14. A Request for Continued Examination (RCE) was filed on April 8, 2005. On May 4, 2005 a third Office Action issued. On November 4, 2005 the Appellants responded to this Office Action by canceling Claim 13 and adding Claims 15-22. A second Final Rejection was mailed on February 6, 2006, wherein the Examiner withdrew Claims 15-22 from consideration. On August 1, 2006 the Appellants responded to the Final Rejection by canceling Claims 21-22. A Notice of Appeal was filed on August 1, 2006.

Claim 1 is pending and on appeal. Claims 2-14 have been cancelled. Claims 15-22 have been withdrawn from consideration.

STATUS OF AMENDMENTS

In response to the Restriction Requirement issued on February 24, 2003, Appellants amended Claim 1, which amendment was entered. Claim 1 was further amended in Appellants response of August 28, 2003, which amendment was entered. Claim 1 was further amended in Appellants response of September 8, 2004, which amendment was entered with the Request for

Continued Examination of April 8, 2005. Claim 1 was further amended in Appellants response of November 4, 2005, which amendment was entered. New Claims 15-22 were also added, and were entered but withdrawn from consideration.

In the response of August 1, 2006, Appellants requested that Claims 21-22 be canceled. This amendment to the claims, however, was not entered by the Examiner as stated in the Advisory Action of November 21, 2006. Accordingly, Claims 21 and 22 are still pending and presently withdrawn from consideration.

SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter is drawn to methods for treating psoriasis.

Independent Claim 1 claims a method for treating psoriasis (see page 4, lines 6-12). The method includes administering an effective amount of an inhibitor of integrin linked kinase (ILK) to a psoriatic lesion (page 4, lines 6-12), wherein the expression of ILK in the psoriatic tissue correlates with the severity of disease (see 4, lines 1-2, and Figures 2A-2D). Additionally, the ILK inhibitor is a small organic molecule that inhibits ILK activity (page 4, lines 28-32).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled.

II. Claim 1 stands rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Bonjouklian in view of the Appellants' own admission and further in view of Zhang.

ARGUMENTS

I. Claim 1is fully enabled.

In this rejection, the Examiner asserts that while Claim 1 is enabled for certain small molecule ILK inhibitor compounds, Claim 1 is allegedly not enabled with respect to all organic small molecule inhibitors.

Specifically, the Examiner asserts that 1) the breadth of Claim 1 is broad in that the claim may encompass *any* small organic molecule inhibitor, 2) the guidance in the specification is allegedly limited, and 3) the quantity of experimentation necessary is allegedly high.

The Appellants disagree. The Appellants submit that one of skill in the art could readily have practiced the present invention as claimed. The present application does not claim to

have discovered methods or compounds for the inhibition of ILK, but rather utilizes various methods well known in the art for the inhibition of ILK, and applies these methods to the novel use of treating psoriasis. Below are the contentions of the Appellants, with respect to the basis of the Examiner's rejection as stated above.

Claim 1 is not overly broad.

Prior to the present invention, small molecule inhibitors of ILK activity as well as methods of utilizing such small molecules to inhibit ILK activity were well known and publicly available. Additionally, one of skill in the art was informed as to assays, multiple model compounds, and guidelines for determining ILK inhibitory activity in a straightforward manner. The level of experimentation to select from among these known methods was routine and readily performed by one of ordinary skill in the art.

Accordingly, the knowledge of one of skill in the art at the time of filing with respect to small molecule ILK inhibitors was high. This is evidenced by the fact that there were several patents issued in the US on small molecular ILK inhibitors: US Patent Nos. 6,214,813 (issued April 10, 2001), 6,291,447 (issued September 18, 2001) and US Patent No. 6,436,915 (issued August 20, 2002). There was also a patent issued on the inhibition of ILK using antisense constructs (US Patent No. 6,177,273) and another issued using antibodies (US Patent No. 6,369,205). Additionally ILK inhibitors known in the art are found in U.S. Patent nos. 7,022,702 (issued April 4, 2006) and 6,420,400 (issued July 16, 2002), which disclose 1,2,3-thiadiazole inhibitors, as well as U.S. Patent no. 6,833,436 (issued December 21, 2004), which discloses short peptides that inhibit serine threonine kinases, including ILK.

Further, in addition to the known inhibitors of ILK, screening programs using known methods were well known in the art and shown to result in the identification of a number of inhibitors of ILK (for example, the molecules described in U.S. Patent nos. 6,214,813 and 6,291,447). Small molecule libraries were available for purchase from companies, such as Talon Cheminformatics (Acton, Ontario) and Asinex (Moscow, Russia), which provided a source of small molecules for ILK inhibition screening. High throughput screening techniques were well known at the time of filing. For example, high throughput screening for inhibitors of ILK was described in US Patent No. 6,214,813 (columns 15-18). Hence, one skilled in the art could identify ILK inhibiting small molecules by running commercially available library compounds through an *in vitro* assay in accordance with published techniques, for instance, using the methods provided in U.S. Patent No. 6,214,813.

Furthermore, methods that utilize inhibition of ILK have been widely published in the scientific literature. For example, one may look to Yau et al. (2005) Cancer Research 65:1497-1504, which tested the anticancer effects of ILK inhibitor QLT0254 in an orthotopic primary xenograft model of pancreatic cancer. Koul et al. (2005) Mol Cancer Ther. 4(11):1681-8 found that a newly developed small-molecule compound (QLT0267) effectively inhibited signaling through the ILK/Akt cascade in glioma cells by blocking the phosphorylation of Akt and downstream targets, including mammalian target of rapamycin and glycogen synthase kinase-3beta. An anchorage-dependent cell growth assay confirmed the cell growth-inhibitory effect of QLT0267. Leung-Hagesteijn et al. (2005) Mol Cell Biol. 25(9):3648-57 demonstrated that treatment with a small molecule ILK inhibitor or expression of a dominant negative-acting ILK (ILK(E359K)) inhibited epithelial cell morphogenesis. Obara et al. (2004) Cancer Lett. 208(1):115-22 found that selective COX-2 inhibitor NS-398 was found capable of down-regulating ILK and PKB/Akt phosphorylation. Persad et al. (2000) Proc Natl Acad Sci U S A. 97(7):3207-12 showed that transfection of a kinase-deficient, dominant-negative form of ILK or exposure to a small molecule ILK inhibitor suppresses the constitutive phosphorylation of PKB/Akt on Ser-473, but not on Thr-308, in the PTEN-mutant prostate carcinoma cell lines PC-3 and LNCaP.

In summary, the Appellants submit that the scope of Claim 1 does not encompass *any* small molecule inhibitor, but rather only those small molecules that inhibit ILK, such molecules being a well known class of inhibitors that were routinely used in the art at the time of the present invention; and which small molecules have subsequently been tested in a number of biologically relevant situations. Therefore, contrary to the assertions by the Examiner, the Appellants contend that the use of the term "small organic molecule that specifically inhibits ILK activity" does <u>not</u> render Claim 1 overly broad.

<u>The specification provides ample guidance as to what is encompassed by the term "small molecule inhibitor of ILK".</u>

In the present application, guidelines are provided for the selection of ILK inhibitors, and for administration instructions, for example at paragraphs 52 and 56 – 69. Experimental models for inflammation are found at Examples 3 and 4, and for psoriasis in particular at Examples 1 and 2. The instant specification teaches the identification of integrin-linked kinase, specific compounds that inhibit the enzyme, and methods of screening for inhibitory agents, and methods of administration on pages 4-14. With respect to the working examples, the inhibitor MC-5 is 4-[(4-fluoro-3-trifluoromethylphenyl)hydrazono]-4H-pyrazole-3,5-diamine, a pyrazole

compound, is shown to be effective in treatment of psoriasis. US Patent No. 6,214,813, referenced on lines 14-15 of page 5 of the present application, offers compounds with similar utility. Therefore, contrary to the assertions by the Examiner, the specification provides ample guidance as to what is encompassed by the term: "small molecule inhibitor of ILK."

The quantity of experimentation is relatively low.

In the present application, data are presented that demonstrate an oral formulation was effective to reduce symptoms of psoriasis in animal models. In view of this evidence, and of the level of skill in the art regarding inhibition of integrin linked kinase, one of skill in the art could readily practice the claimed invention, with no more than routine formulation skill or experimentation. A person skilled in the art would be able to take the compounds disclosed in the art discussed above, for instance, U.S. Patent Nos. 6,214,813; 6,291,447; 6,436,915 (pryazoles) and 6,291,447 (granulatimides), as well as U.S. Patent Nos. 6,001,622 (wortmannin) and 7,022,702 (1,2,3-thiadiazoles), and apply them to the claimed method, using the information supplied in those patents and in the present application on pages 6-15 and 16-17.

Consideration of the Wands factors.

The legal test for whether a disclosure provides adequate enablement for a generic claim is that "the scope of the claims must bear a *reasonable correlation* to the scope of enablement provided by the specification to persons of ordinary skill in the art." *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. (BNA) 18, 24 (C.C.P.A. 1970) (emphasis added), *cited with approval in Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1212, 18 U.S.P.Q.2d (BNA) 1016, 1026 (Fed. Cir. 1991).

To evaluate the scope of enablement provided by a specification, the proper standard is whether any experimentation that may be needed to practice the claimed invention by the skilled artisan is undue or unreasonable. *In re Wands*, 858 F.2d at 736-37, 8 U.S.P.Q.2d (BNA) at 1404 (Fed. Cir. 1988). Whether a claim is enabled is a question of law based on underlying factual findings. *Wands*, 858 F.2d at 735, 8 U.S.P.Q.2d (BNA) at 1402. *Wands* sets forth the relevant underlying fact inquiries:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. 858 F.2d at 737, 8 U.S.P.Q.2d (BNA) at 1404.

Thus, the requirement that the patent holder enable the "full scope" of the claimed invention has never been interpreted to require the enablement of every embodiment within the scope of the claims. *See, e.g., In re Wright*, 999 F.2d 1557, 1563, 27 U.S.P.Q.2d (BNA) 1510, 1515 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d (BNA) 1438, 1445 (Fed. Cir. 1991) ("It is well settled that patent Appellants are not required to disclose every species encompassed by their claims, even in an unpredictable art.") (citation omitted); *Hormone Research Found. v. Genentech, Inc.,* 904 F.2d 1558, 1568, 15 U.S.P.Q.2d (BNA) 1039, 1047-48 (Fed. Cir. 1990); *Durel Corp.,* 256 F.3d at 1306, 59 U.S.P.Q. (BNA) at 1244 (accused product within scope of claims need not be enabled; patent is enabling even if it fails to enable a "significant percentage" of embodiments within the scope of the claims). In *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 750 F.2d 1569, 224 U.S.P.Q. (BNA) 409 (Fed. Cir. 1984), the court made clear that the full scope of a claim is enabled even if there are "significant" portions of the claim which are not enabled provided the person of ordinary skill can practice the invention without undue experimentation:

What is required is that "reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d at 1366, 42 U.S.P.Q.2d (BNA) at 1005 (Fed. Cir. 1997). According to *Novo Nordisk*, the essence of the enablement inquiry is that the inventor must teach how to make and use *the novel aspects of an invention. Id.*, 42 U.S.P.Q.2d (BNA) at 1005.

When determining the scope of enablement provided by an application, the law is clear that an enabling teaching may be provided "through broad terminology or illustrative examples." *In re Wright*, 999 F.2d at 1561, 27 U.S.P.Q.2d (BNA) at 1513; *see also In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. (BNA) 367, 369 (C.C.P.A. 1971). An express disclosure of only one illustrative example, such as a method of making one embodiment within the scope of the claimed invention, may be enough to enable the full scope of the claimed invention. *See Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1359-61, 47 U.S.P.Q.2d 1705, 1717 (Fed. Cir. 1998); *United States v. Telectronics, Inc.*, 857 F.2d 778, 786, 8 U.S.P.Q.2d (BNA) 1217, 1223 (Fed. Cir. 1988); *In re Wands,* 858 F.2d 731, 737, 8 U.S.P.Q.2d (BNA) 1400, 1407 (Fed. Cir. 1988).

To support a finding of non-enablement, the U.S. Patent and Trademark Office must establish a reasonable basis to question the enablement provided in the specification. *In re Wright*, 999 F.2d at 1562, 27 U.S.P.Q.2d (BNA) at 1513. The Office must not only explain why it doubts the statements in the specification's supporting disclosure, but also must support its assertions "with acceptable evidence or reasoning which is inconsistent with the contested

statement." *In re Marzocchi*, 439 F.2d at 224, 169 U.S.P.Q. (BNA) at 370. The Office is required to consider the factual evidence in favor of enablement in the record. *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d (BNA) 1578, 1583 (Fed. Cir. 1996). When an applicant requests reasonable factual support for an Examiner's rejection, the Examiner must provide it under 37 C.F.R. § 1.104(d)(2). The Board is not obligated to accept as fact any statements of the Examiner that are not adequately supported in the record. *Application of Lundberg*, 244 F.2d 543, 551, 113 U.S.P.Q. (BNA) 530, 537 (C.C.P.A. 1957). Indeed, the Board should not accept as fact any of the Examiner's statements that lack support in the record. *Dickinson v. Zurko*, 527 U.S. 150, 154 (1999).

The present specification enables one of ordinary skill in the art to practice the method set forth in Claim 1. The consideration of Wands factors are as follows.

Wands Factor 1. Any experimentation required to have practiced the invention of claim 1 is quite low.

As discussed above, compounds for inhibition of ILK and methods for their use were known in the art at the time of filing the present application. One need only optimize dose and formulation for practicing the invention. As such, the only experimentation that may be required is to perform routine procedures to determine the appropriate dose of a certain activity. Since such experiments are empirical in nature, no undue experimentation is required.

Wands Factor 2. The specification provides significant guidance to the skilled worker for practicing the invention of Claim 1.

As discussed in detail above, one of skill in the art was well-informed as to inhibitors of integrin linked kinase at the time of filing the present application. Specific guidelines for the administration of such compounds is provided in the specification, for example at paragraphs 52 and 56 – 69. The instant specification teaches the identification of integrin-linked kinase, specific compounds that inhibit the enzyme, methods of screening for inhibitory agents, and methods of administration on pages 4-14.

Wands Factor 3. The instant specification contains working examples that demonstrate embodiments of the invention claimed, including the actual cloning of human ILK and the use of the protein as an immunogen.

Experimental models for inflammation are found at Examples 3 and 4 and for psoriasis in particular at Examples 1 and 2. Therefore, it is demonstrated that treatment of psoriasis can be effected by administration of an integrin linked kinase inhibitor.

Wands Factor 4. The nature of the invention claimed is treatment of psoriasis via the administration of an ILK inhibitor.

Contrary to the statement made by the Examiner, the claims are not drawn to a method for treating psoriasis by the administration of *any* small molecule, but to the treatment of psoriasis via the administration of an ILK inhibitor molecules, which molecules are well known in the art.

Wands Factor 5. The state of the art in December 1995 was quite sophisticated.

As acknowledged by the Examiner on page 8 of the Final Rejection issued February 6, 2006, "the state of the art regarding "a small organic molecule" and its subsequent testing as an inhibitor of ILK or any receptor is high."

Wands Factor 6. In November 2001, the level of skill in the art was high.

The routine level of skill in the field of recombinant nucleic acid technology in November 2001 was represented by a scientist with a Ph.D. degree and two years of post-doctoral training. Furthermore, such technicians are required to keep abreast of the latest technology through continuing education and reading of scientific journal articles. As such, the skill level of those developing and using methods for manipulating and performing cell-based assays is high. Such a person would have considered it routine to select from available compounds or to screen libraries of compounds using the common general knowledge, tools, and methods available in the field.

Wands Factor 7. Utilizing various known compounds or screening libraries of compounds against a known target using published methods was predictable.

The amount of experimentation required to treat psoriasis using compounds that specifically inhibit integrin-linked kinase, as identified by Appellants, would not be undue because a) examples of inhibitors are provided, b) guidance is given on how to screen for additional inhibitors, and c) one of skill in the art would be able to perform the experiments as a matter of routine to determine the optimal dosage in view of the teachings in the Appellants disclosure.

Wands Factor 8. Breadth of Claims.

With respect to the breadth of the claims, as described above, the breadth of the Claim 1 is commensurate with the scope of the invention in light of what was previously known in the art. It is believed that the Appellants are entitled to this scope for this reason.

Conclusion

It is the factual inquiries set forth in *In re Wands* that determine undue experimentation. As can be seen with respect to the consideration of the Wands factors set forth above, the enablement of Claim 1 provided by the instant specification is reasonably commensurate with the scope of all the claims. See *In re Fisher*, 427 F.2d at 839, 166 U.S.P.Q. (BNA) at 24, *cited with approval in Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d at 1212, 18 U.S.P.Q. 2d (BNA) at 1026. The inventors have taught how to practice all the claimed features of their invention. See *W. L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d at 1557, 220 U.S.P.Q. (BNA) at 316.

Therefore, the Appellants contend that the present claim(s) meet(s) the requirements of 35 U.S.C. § 112, first paragraph, with respect to enablement and request that this rejection be reversed.

II. Claims 1 is not obvious under 35 U.S.C. §103(a) over Bonjouklian et al. in view of the Appellants' own admission and further in view of Zhang et al.

In this rejection, the Examiner asserts that the claim(s) are rendered obvious over Bonjouklian in view of the Appellants' own admission and further in view of Zhang. In sustaining this rejection, the Examiner asserts that Bonjouklian discloses the use of wortmannin (an inhibitor of phosphatidylinositol 3-kinase) for the treatment of PI 3-kinase dependent biological processes.

However, the Examiner acknowledges that Bonjouklian does not teach that wortmannin is an inhibitor of ILK or the use of wortmannin for the treatment of psoriasis. The Examiner, therefore, relies on the Appellants own admission and Zhang to remedy the deficiencies of Bonjouklian.

In response, the Appellants respectfully submit that according to the M.P.E.P. § 2143 to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine

reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

It is respectfully submitted that the Examiner's *prima facie* case of obviousness is deficient because the recited combination fails to teach or suggest every element of the rejected claims, there is no motivation to combine the references in the manner suggested and there is no likelihood of success in the Appellants' claimed invention. Below are the contentions of the Appellant with respect to the grounds of rejection as stated above.

The presently claimed invention is based on the finding that integrin linked kinase (ILK) is correlated with the severity of psoriatic lesions, as shown in Figures 1 and 2. Psoriasis is a complex inflammatory autoimmune condition characterized by an abnormal activation of skin T lymphocytes, dermal and epidermal infiltration by various types of leukocytes, hyper-proliferation of keratinocytes and pronounced angiogenic activity within the dermal vasculature. Prior to the instant invention, it was unknown whether the activity or expression levels of ILK were altered in the specific human pathologic states resulting from psoriasis.

As shown in Figure 1, a low level of ILK expression is seen in normal keratinocytes, and little or no ILK staining occurs in the dermal vascular endothelium. In contrast, staining for ILK was found to be highly intense for the hyper-proliferative keratinocytes within psoriatic plaques. Further, some of the inflammatory cells present within the dermal region stained positively for ILK. Overall, in contrast to normal skin, ILK was expressed at much higher levels within the epidermal and dermal regions within skin plaques of patients with psoriasis.

Bonjouklian, the primary reference, discloses that wortmannin and analogs thereof are inhibitors of phosphatidylinositol 3-kinase. The claims of Bonjouklian reflect this specificity and are directed to methods of treating a phosphatidylinositol 3-kinase-dependent neoplasm in a mammal by administering to the mammal wortmannin or an analog thereof.

Zhang, the secondary reference, discloses that there is an increase in expression of PI(3)kinase in psoriatic lesions as evidenced by non-quantitative methods of immunohistochemistry, *in situ* hybridization, and dot blot analysis. The reference states that PI(3)-kinase *may* be correlated with hyperproliferation of psoriatic keratinocytes, but that "further studies are required to elucidate it".

Accordingly, Zhang fails to remedy the deficiencies of Bonjouklian because Zhang fails to teach an association of integrin linked kinase with psoriasis, fails to teach the treatment of psoriasis with an inhibitor of integrin linked kinase, and even fails to teach the treatment of psoriasis by inhibition of PI(3)kinase.

Therefore, the Appellants contend that a *prima facie* case of obviousness has not been established because the combination of Bonjouklian and Zhang fail to teach or suggest all the elements of the rejected claim(s), namely, the administration of an inhibitor of ILK for treating psoriasis. As explained above, the cited references fail to teach or suggest this because Bonjouklian merely discloses the use of wortmannin as a PI(3)kinase inhibitor and Zhang merely discloses that there is an increased expression of PI(3)kinase in psoriatic lesions, however, neither reference, alone nor in combination, teach or suggest an association of integrin linked kinase with psoriasis, or the treatment of psoriasis with an inhibitor of integrin linked kinase. For this reason alone this rejection should be reversed.

The Examiner, however, impermissibly relies on the Appellants' teachings for drawing a connection between the use of wortmannin and the treatment of psoriasis. The Examiner asserts that on page 5 of the Appellants own specification, the Appellants teach that ILK activity is down regulated by inhibiting PI(3) Kinase and that wortmannin may be used to inhibit PI(3) and thereby inhibit the activity of ILK.

The Appellants disagree with the reasoning of the Examiner and would like to draw the attention of the Board to M.P.E.P. § 2142, which states that although the tendency to resort to "hindsight" based upon the Applicant's disclosure is often difficult to avoid, due to the very nature of the examination process, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.

In the present case, the Examiner is clearly relying on the Appellants' own disclosure for the teaching that wortmannin may be used to inhibit the activity of ILK and to treat psoriasis. Accordingly, the Examiner is not relying on facts gleaned from the prior art but rather on facts derived from the Appellants' own specification and is, therefore, impermissibly relying on hindsight reasoning in contravention of M.P.E.P. § 2142. For this reason alone this rejection should be reversed.

Additionally, even if one could combine the references in the manner suggested, a *prima facie* case of obviousness has still not been established because at most all that would be derived is an invitation to try and not a likelihood of success in the Appellants claimed invention. One of skill in the art simply could not reasonably expect to be in possession of the presently claimed invention based on the combination of cited references. Even assuming that there is an increase in PI3 kinase associated with psoriasis, the art does not teach that such an increase is associated with disease progress or could be inhibited (e.g., by the application of wortmannin) to provide treatment of psoriasis. Therefore, for this reason alone this rejection may be reversed.

The Examiner, however, points to M.P.E.P. § 2112 and asserts that the discovery of a previously unappreciated property of a prior art composition does not render the old composition patentably new to the discoverer. However, the Appellants would like to point out that M.P.E.P § 2112 also states that "[a]n invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367, 71 USPQ2d 1081, 1091 (Fed. Cir. 2004) (explaining that "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species.

Accordingly, simply because Bonjouklian discloses wortmannin for use as an inhibitor of phosphatidylinositol 3-kinase does not mean that Bonjouklian inherently discloses the use of wortmannin as an inhibitor of ILK activity or its beneficial use for the treatment of psoriasis. Rather, according to M.P.E.P. § 2112, to establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." The Examiner, however, has not shown how Bonjouklian's disclosure of wortmannin as a phosphatidylinositol 3-kinase inhibitor necessarily means that wortmannin is an inhibitor of ILK activity or that it can necessarily be used to treat psoriasis. Hence, as described above, the Appellants submit that one of skill in the art could not reasonably expect to be in possession of the presently claimed invention based on the combination of the cited references.

Conclusion

Therefore, in view of the above, a *prima facie* case of obviousness has not been established because the cited combination does not 1) teach or suggest all of the elements of the claimed invention, namely, the administration of an inhibitor of ILK for treating psoriasis; 2) provide a motivation to combine; or 3) establish a likelihood of success in the Appellants claimed invention. Consequently, the Appellants respectfully request the reversal of this rejection.

SUMMARY

I. Claim 1 meets all the requirements for enablement as recited under 35 U.S.C. § 112, first paragraph.

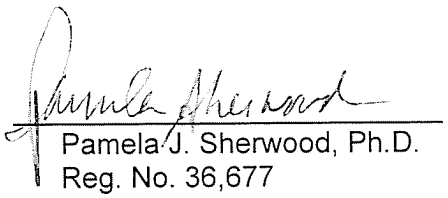
II. Claim 1 is not obvious under 35 U.S.C. 103(a) over Bonjouklian in view of the Appellants' own admission and further in view of Zhang.

RELIEF REQUESTED

Appellant respectfully requests that the rejections of Claims 1 and 15-22 be reversed and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance. The Commissioner is authorized to charge any fees that may be required, or credit any overpayment to Deposit Account 50-0815 order number KINE-001 CIP5.

Respectfully submitted,
Bozicevic, Field and Francis LLP

Date: December 10, 2007



Pamela J. Sherwood, Ph.D.
Reg. No. 36,677

Bozicevic, Field and Francis LLP
1900 University Avenue Suite 200
East Palo Alto, CA 94303
(650) 327-3400 (P)
(650) 327-3231 (F)

CLAIMS APPENDIX

1. A method for treating psoriasis, the method comprising:

administering an effective amount of an inhibitor of integrin linked kinase (ILK) to a psoriatic lesion, wherein expression of ILK in psoriatic tissue correlates with severity of disease, and said ILK inhibitor is a small organic molecule that inhibits ILK activity.

EVIDENCE APPENDIX

No evidence that qualifies under this heading has been submitted during the prosecution of this application, and as such it is left blank.

RELATED PROCEEDINGS APPENDIX

As stated in the *Related Appeals and Interferences* section above, there are no other appeals or interferences known to Appellant, the undersigned Appellant's representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal. As such this section is left blank.